Inertial wearables as pragmatic tools in dementia

A Godfrey[1], M Brodie[2,3], KS van Schooten[4,5], M Nouredanesh[6], S Stuart[7], L Robinson[8]

[1] Department of Computer and Information Science, Northumbria University, Newcastle, UK
[2] Falls Balance & Injury Research Centre, Neuroscience Research Australia, NSW, Australia
[3] Graduate School of Biomedical Engineering, University of New South Wales, NSW, Australia
[4] Neuroscience Research Australia, University of New South Wales, Sydney, Australia
[5] School of Public Health and Community Medicine, University of New South Wales, NSW, Australia
[6] Department of Mechanical and Mechatronics Engineering, University of Waterloo, Waterloo, Canada
[7] Department of Neurology, Oregon Health & Science University, Portland, Oregon, USA
[8] Institute for Ageing, Newcastle University, Newcastle upon Tyne, UK

Corresponding author
Alan Godfrey BEng, PhD, MBA
Department of Computer and Information Science,
Northumbria University,
Newcastle upon Tyne,
NE1 8ST,
UK
Tel: 0191 227 3642
Email: alan.godfrey@northumbria.ac.uk

Highlights

- Dementia is an important issue with an ever greater impact on society.
- Wearable devices are now widely discussed as useful pragmatic tools in neurodegenerative diseases.
- Inertial wearables can quantify postural control and gait to provide useful digital biomarkers in dementia.
- Lack of standards and lack of access to large data sets are limiting the use of wearables in modern medicine.

Abstract

Dementia is a critically important issue due to its wide impact on health services as well as its personal and societal costs. Limitations exist for current dementia protocols, and there are calls to introduce modern technology that facilitates the addition of digital biomarkers to routine clinical practice. Wearable technology (wearables) are nearly ubiquitous in everyday life, gathering discrete and continuous digital data on habitual activities, but their utility in modern medicine remains low. Due to advances in data analytics, wearables are now commonly discussed as pragmatic tools to aid the diagnosis and treatment of a range of neurological disorders. Inertial sensor-based wearables are one such technology; they offer a low-cost approach to quantify routine movements that are fundamental to normal activities of daily living, most notably postural control and gait. Here, we provide a narrative review of how wearables are providing useful postural control and gait data to facilitate the capture of digital markers to aid dementia research. We outline the history of wearables, from their humble beginnings to their current use beyond the clinic, and explore their integration into modern systems, as well as the ongoing standardisation and regulatory efforts to integrate their use in clinical trials.

Keywords: big data; diagnostic; gait; inertial sensor; postural control

1.0 New approaches in dementia

Dementia is a common disorder in older adults where the major subtypes include Alzheimer's disease and vascular dementia [1]. Traditional tests designed to diagnose neurodegenerative disorders are often delayed in detecting abnormalities in cognitive decline in the earliest stages of the disease [2]. Hence, there is a need for robust pragmatic and objective tools to aid clinical decisions.

Dementia and cognitive decline are associated with significant gait [3] and postural impairments (including slow gait speed, increased variability, inability to dual-task, and increased postural sway) [4], which are further associated with poor health and mortality [5]. A recent meeting of the Alzheimer's Association Research Roundtable [6], discussed how wearables and their digital biomarkers are transforming clinical trials with emerging efforts to apply lessons learned in other diseases (e.g. multiple sclerosis and Parkinson's disease) to the dementia clinical trial space. Topics of discussion included how wearables can improve screening, engagement and compliance with treatment, while providing new insights towards personalised medicine [7].

Inclusion of wearables as viable tools in clinical studies is growing due to increased sensing capabilities. They are revolutionising medical capabilities to measure beyond the clinic, providing real world data capture during habitual activities in everyday life on a truly global scale [8]. However, not entirely without the caveat of reduced accuracy from the use of unvalidated technologies [9]. Steps to modernise medicine have seen wearables become smaller, cheaper and ergonomically pleasing, affording extended wear time for nearly all ages in most environments. This drives trends towards digital biomarkers/outcomes/parameters stemming from consumer grade technologies [2]. Here we present recent applications of wearables that may be utilised in dementia. This paper presents and discusses how inertial sensor-based wearables currently quantify pragmatic human movement data (postural control, PC and gait) to drive innovation in this field across different themes (Figure 1).

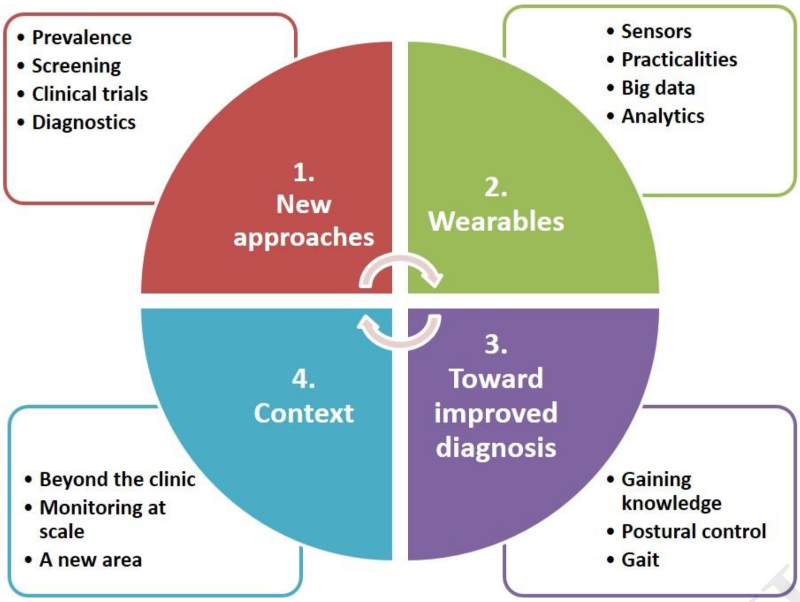

Figure 1: Considerations for implementation of digital technology in dementia care

2.0 Wearables

2.1 From humble beginnings towards pragmatic clinical tools

Current interests and trends in wearables (including smartphone) relate to their use as viable mobile diagnostic tools providing digital clinical-based biomarkers [10]. A plethora of research has erupted with the use of inertial sensors. Accelerometers can be used to capture human movement in substantial detail across a range of biomechanical configurations; accuracy may be enhanced through data fusion with gyroscopes and global positioning systems [11], barometers to detect height changes (associated with postural transitions [12], falls [13] or stair climbing [14]) or cameras to provide situational context [15]. The use of inertial sensors has led to instrumented versions of traditional tests (e.g. timed-up-and-go, TUG), offering more than just total time to complete a task, including high-resolution spatio-temporal data at millisecond precision [16, 17].

The proliferation of wearables in healthcare aims to make clinical trials more efficient and less burdensome to participants (and staff), contributing to a meaningful and real-world understanding about the patient's performance beyond any brief ''snapshots'' ordinarily gathered in clinical care or research settings [18]. To date, single tri-axial accelerometer-based wearables remain the most common sensor to quantify gait and PC data [19, 20]. Increasing sensing capabilities with a gyroscope come with a technical (battery life and memory storage capabilities) and pragmatic (wearable size and deployment time) trade-off. Typically, wearables sample/gather movement up to 100 data point per second (100-Hertz, Hz), depending on the activity to be measured. Assuming the need for a comprehensive assessment at 100Hz for seven consecutive days, a single tri-axial accelerometer-based wearable will gather >181-million data points[1]. Assuming two bytes per sample for each tri-axial signal, this equates to 362MB of data/week for one participant. Given the scenario of a large study (n=100) with repeated (pre, post and long-term follow up) 7-day assessments, this could generate approximately 109GB, big data.

2.2 Big data

Although the definition of big data is vague, it is classed as any data approximately 1 petabyte (PB[2]) but in wearable and health research in general, data of that size is rare [21]. Widespread acceptance of wearables has led to larger data sets becoming available including the Azumio Argus smartphone dataset comprising 68 million days of PA for 717,527 people across 111 countries (available from Stanford University) [8], and the 7-day Axivity AX3 wrist-worn tri-axial accelerometer dataset from 100,000 people in the UK (available from UK Biobank) [22]. The later dataset could be linked to health records, assessment of the built environment and other assessments including brain imaging [23, 24]. Combing these technologies would provide new opportunities to study the complex relationship between characteristics of human movement and dementia.

Fundamental challenges of big data are evident with inertial sensors within wearables and mobile devices where the latter utilise unregulated and unverified applications/apps [25]. Specifically, the consumer-grade devices often used for large-scale monitoring [8] are unsuitable to detect steps in people with slow or short walks [9], such as people with dementia [26]. Monteith et al [27] discuss big data complexity and present the "large *n*, small *p*" problem, based on traditional clinical trials having a large number of subjects (*n*) compared to a small number of biomarker (*p*). Big data (derived from wearables and smartphones) alter that relationship to "large *p*" due to the ability to quantify a range of novel biomarker, creating demanding computational and statistical challenges for analysis and interpretation [27, 28]. Monteith et al also raise the perspective that big data defines one's ability to analyse and formulate decisions, i.e. making sense of data. Transforming big data into smart data through new integrative mechanism-based predictive platforms could help further the development of effective treatments for the dementias, creating actionable outcomes to yield patient orientated benefits [29].

2.3 Analytics

Dinov et al [30] describe (predictive) big data analytics by referring to algorithms, systems and tools that use big data to extract information, generate maps, prognosticate trends, and identify patterns

[1] 100 data points per second * 60 (seconds) * 60 (minutes) * 24 (hours) * 7 (days) * 3 (axis)
[2] 1PB = 10^6 GB

in a variety of past, present or future settings. Methodologies used to perform these tasks should make the underlying patterns transparent to the person who tries to utilize and understand them [31]. The complexity of neurodegenerative diseases generates significant heterogeneity of data in that area, where analytical processes can make use of a wide range of big data integration, modelling and mining strategies in order to understand and make predictions in complex systems [32]. Machine learning approaches including density estimation methods and dimensionality reduction are suitable for modelling patterns and correlations in data, discovering relationships and making predictions based on unseen events. Additionally, novel techniques such as fuzzy logic and artificial neural networks are more readily used to address complex real-world data from stochastic processes where traditional modelling approaches are unable to work due to high complexity and uncertainty [31]. Recent work presents data handling techniques to analyse and contextualise wearable data from numerous streams (e.g. wearables, ambient sensors) described as a personalised ambient assisted living framework for those with dementia [33, 34]. The benefit of such a multimodal data handling ensures a holistic approach to care while offering opportunities for clinicians and caregivers for remote monitoring needs [35].

3.0 Towards improved diagnosis

3.1 Gaining knowledge

Fundamental components of modelling human movement through inertial sensor-based wearables centres on static and dynamic conditions. The former encapsulated by sedentary periods of inactivity such as sitting and lying as well as upright periods of standing. Maintaining PC and spatial orientation during standing is reliant on a healthy vestibular system, integral to sensory-motor function [36]. Recommendations suggest the use of a single accelerometer-based wearable on the lower back is optimal (time, cost) for measuring balance and screening for vestibular impairment [36, 37].

Winter [38] describes standing as one’s ability to keep their body’s centre of mass safely within the base of support but when initiating, maintaining and terminating walking, conditions are radically transformed to complex dynamic balance situations. Walking may have once been considered a routine and simple task of daily living but is now hotly discussed as a pragmatic tool: a window into brain functioning for neurological conditions [39]. Walking is regularly defined by two similar conceptual gait models [40, 41] describing: (i) macro/quantity based on broad trends in the wearable data comprising behavioural aspects (e.g. walking duration); and (ii) micro/quality, step-by-step characteristics defined by spatio-temporal and frequency measures (e.g. step time, harmonic ratio).

The pragmatic approach adopted by Lord et al [41, 42], originating from laboratory-based work, present 16 micro spatio-temporal gait characteristics mapped to 5 domains: pace (3), rhythm (3), variability (4), asymmetry (3) and PC (3). However, the inability of a wearable placed on the lower back (5th lumbar vertebrae, L5) to measure step width and step width variability means PC domain omission under free-living conditions and loading of the third PC characteristic (step length asymmetry) to the asymmetry domain [43]. As the use of models developed in the laboratory shift to deployment in habitual environments, the loss and restructuring of pragmatic PC biomarker within gait is less than satisfactory. Perhaps this could be ameliorated by the inclusion of novel data and techniques afforded by wearables during dynamic conditions.

3.2 Postural control

A recent (2017) systematic review by Mesbah and colleagues examined PC (termed postural stability by the authors) in older adults with Alzheimer's disease [44]. Of the eighteen studies included, only one used a wearable (accelerometer and gyroscope) suggesting the uptake of wearable devices has been delayed in this cohort. In the small study identified, a group of 11 fallers and 9 non-fallers were compared to healthy controls under different conditions for 30-seconds (including flat, frontward and backward inclined surfaces) [45]. Authors found signs of impaired PC in those with Alzheimer's disease, due to higher mediolateral/anteroposterior (ML/AP) range of sway and a constant need for more corrections of centre of mass pitch and roll angles. Another study investigated virtual reality goggles to induce the illusory perception of falling and assessed PC using a wearable accelerometer [46]. That study found slower reaction compensatory balance reactions for those Alzheimer's disease compared to healthy subjects. Of note were the use of time-frequency data where the authors noted how that might provide further information about neurological mechanisms.

Wearables have been used during real-time feedback during balance training in 11 people with mild cognitive impairment with 92% acceptance rates [47]. Wearable assessment of PC combined with machine learning was explored as a tool for diagnosing Alzheimer's disease. Costa et al. [48] found increased accuracy (91%-96%) was possible when the Montreal Cognitive Assessment scores were combined with the postural kinematics. Elsewhere, wearable assessment of sway speed explored differences between those with Alzheimer's disease and healthy subjects [49]. For those with Alzheimer's, postural sway in the ML direction (tandem and single stance) was found to be more sensitive than in the AP direction. These studies show valuable insight to the use of wearables in PC assessment but larger prospective studies in people with dementia are required.

3.3 Gait

Gait has generated significant interest due to its complex multifaceted nature and associations to different brain activation patterns. For example, a recent review investigated structural and functional neuroimaging findings for those with dementia, describing gait variabilities important role for sensorimotor integration and coordination [50]. As with most conditions, early detection in low-resource settings to evoke suitable interventions is of primary concern. Evidence suggests that reduced gait speed, manually derived by time to walk a set distance, occurs early in dementia and may precede decline on cognitive tests [51]. A recent multifactorial approach included gait speed assessment within a clinical-based study using an instrumented walkway, diagnosing the motoric cognitive risk (MCR) [52] syndrome: a streamlined approach identifying those at risk of developing dementia. That large study (17 countries with 22 cohorts resulting in 26,802 individuals) showed MCR was associated with increased cognitive impairment but reported heterogeneous gait speed methods of assessment including instrumented and manual times, highlighting the need for more standardised approaches. Yet, the long-term associations between gait speed and dementia risk have also been explored with evidence of dementia in those with reduce gait speed up to 7-years prior to its clinical onset [53, 54]. Considering a more holistic cognitive and physical functioning approach incorporating a range of assessments (e.g. TUG, instrumented PC) found a significant decline in performance over one year in older people with mild to moderate dementia [55].

4.0 Context

Instrumented walkways have been a common method to quantify spatio-temporal gait data. Their mainstream use and standard/uniform quantification approach facilitate pooling of data. For example, examining cross-sectional studies from seven countries found spatio-temporal outcomes deteriorated due to progression from MCI to moderate dementia and are more affected in non-Alzheimer's than in Alzheimer's [56]. The study also showed differences between subgroups (e.g. AD vs. non-AD) are more noticeable in later stages of dementia for the majority of biomarker such as stance time, stride length or stride length. Of note, non-Alzheimer's subjects presented the highest effect size in both subtypes of dementia in the mild and the moderate stages. Three dimensional motion analysis systems have also been used to investigate spatio-temporal (and joint excursion) biomarker under single and dual task conditions in those with Alzheimer's disease and behavioural variant of frontotemporal dementia, showing worsening in Alzheimer's type dementia when cognitive resources are stressed [26].

Typically, studies adopt linear walking protocols which, although useful to examine initial gait hypothesis, lack insight to replicate habitual limitations. Those with dementia have impaired executive functioning and struggle with initiation, planning and attention in goal-directed movements [57]. Thus, increasing gait task complexity is a means of evaluating the effect of cognition on performance [58]. Hunter and Divine [59] tested that theory by manually assessing gait speed in those with Alzheimer's disease on a curved path, showing a significant deterioration in performance (reduced time) compared to straight line walking. However, assessments performed under observation and use of instrumented walkways are limited, snapshot evaluations in unnatural environments. Wearable-based approaches can be more beneficial as evidence from a recent 14-month pilot study found dynamic PC outcomes versus (manually computed) gait speed and stride time better correlated to future cognitive decline [60]. Thus, the use of wearable facilitates new and habitual measurements for of PC and gait in dementia beyond the clinic.

4.1 Beyond the clinic: Towards remote monitoring

Wearable gait data collected under free-living conditions over 3-days can highlight differences in fall-risk between fallers and non-fallers [61]. Additionally, 7-day wearable data has contributed to the identification of individuals at risk of falls compared to lab-based assessment [25] or even predicted falls in 6 months [62]. Yet, compared to other cohorts, most free-living gait studies conducted in people with dementia have been small (n=24, 20 and 10) [63-65], focusing on the feasibility of remote monitoring. Twenty-four hour habitual use of a single wearable (waist mounted device) unexpectedly showed a faster gait cycle for those with Alzheimer's disease compared to healthy controls [63]. The authors hypothesised that these differences possibly reflect reduced Alzheimer's disease consciousness to either the environment or instability of gait. Two larger dementia studies (n=77 and n=45) showed average walking bout duration derived from 24-hour and 7-day physical activity data was an independent predictor of falls [66] and demonstrated those with dementia are less active in daily-life and present with significant impairments across multiple gait domains including gait speed [67], respectively. In contrast another study reported gait speed was less sensitive to identify those with dementia [65]. However, author's remark groups were not aged matched and recruitment periods were different (dementia in summer vs. controls in winter). This highlights environmental factors which may subtly influence free-living gait assessment in those with dementia and may need to be considered when delivering interventions and follow-up assessments at scale.

4.2 Monitoring at scale

A recent sub study with the Dementia Platform UK[3], explored gait (with a single wearable) as a potential clinical (bio) marker within the Deep and Frequent Phenotyping for Experimental Medicine in Dementia Study [64]. As well as administrating a battery of other tests, this study examined upskilling by clinical staff new to this field to deliver repeated wearable gait assessment, including multiple laboratory and 7-day raw data downloading and file transfer via an online service to a remote institution for local analysis. The feasibility work (n=20 people with dementia) showed the ability to collect macro and micro AD-based wearable gait data at scale in accordance with other clinical scales from six UK centres. That approach could be further improved/streamlined with cloud-based analytics, offering more efficient gait (or other) analysis [68].

Suggestions for routine deployment and use of wearables within communication networks for generic healthcare assessment have been widely proposed for many years. Yet, establishing such systems remains problematic due to complexities surrounding system integration, data transfer and protection and most significantly, financial cost. Although impractical to deliver at scale, current developments present interesting proposals to integrate wearables within ubiquitous sensing environments by harnessing the power of the Internet of Things. A recent example to complement wearable data with contextual information is presented by Pham and colleagues [69]. Although the authors deploy a suite of wearables, of interest were the use of a commercial smartwatch and a bespoke inertial device (thigh) using an open source Cloud Orchestration Software (OpenStack Juno) consisting of distinct components/layers to (i) gather/configure, (ii) analyse, (iii) interpret and (iv) store wearable data. ML approaches automated activity recognition by examining time and frequency features of wearable data. Combined with wall mounted passive infrared sensors, individuals were tracked and monitored around the test environment for the purposes of interacting with a mobile robot prototype, which reminds the individual to stay hydrated. Such systems could be important for remote monitoring and safeguarding of frail adults or those with cognitive impairments to deliver useful prompts to undertake activities of daily living. Moreover, wearable integration/communication with passive environmental sensors may help provide contextual information relating to a serious to adverse event, e.g. fall. Alternatively, those with dementia often experience restlessness/agitation and heightened stress [70]. Numerous wearable data streams including inertial, heart rate, microphone, temperature and environmental light have been collected to determine effectiveness for measuring agitated behaviour with some success [71, 72].

Efforts to control cost while enabling flexible contextual and real-time analysis, integrating new digital infrastructures with existing information systems to easily share data between stakeholders in any environment were recently explored. Curry et al. [73] present a "pay-as-you-go"

[3] www.dementiasplatform.uk

based approach rationalised by the overarching principle that the publisher of the data is responsible for paying the cost of joining the system, facilitating participants subscribing or leaving at any time. This flexible style could address long-term “buy-in” while resolving concerns relating to efficient energy consumption and data collection. Those issues raise concerns of how wearables are powered for longitudinal use, knowing when and where to record or propagate data to the cloud [74]. Redmond et al. [75] state the need for smarter wearables able to pre-process data and extract salient information before transmission, preserving battery life. Yet, the authors note that this approach results in certain forms of information loss. Hence, knowing *what to measure* becomes extremely important to maximise data capture while preserving wearable usage time.

4.3 Digital biomarker: A new era

The abundance of wearables in health related studies has proliferated the accumulation of new digital-based biomarker, which may provide new insight for patient treatment [76]. Innovation, led by new multi/cross-disciplinary research has broadened the range of digital biomarkers (large *p* – section 2.1). From the often-blunt metrics of (e.g.) total walking time or step count, high-resolution spatial and temporal biomarker are now realised and used with some degree of confidence, showing disease-specific changes in free-living walking/gait [77]. Elsewhere, a difference in wearable physical activity counts for those within a heart failure intervention compared to a placebo was identified, but not by the traditional regulatory-accepted patient-reported biomarker [78]. Certainly, this is cause for optimism as medicine seeks to rationalise new patient-focused outcomes in real-life scenarios for more informed diagnosis and treatment.

5.0 Closing the loop

Advances in wearables and associated algorithms can often be overwhelming for clinical-based researchers but expert guidance exists. Of note are recent efforts by the Clinical Trials Transformation Initiative[4] (CTTI), a partnership of more than 80 organisations including government (e.g. Food and Drug Administration), industry representatives (e.g. pharmaceutical) and academic institutions. Recently, CTTI systematically reviewed and catalogued the breadth of wearable/mobile-based feasibility studies to enable the development of clinical trials that will use these technologies [79]. Subsequently, CTTI created an online, searchable database aiming for it to become a widely used tool, promoting standardisation of methodology and reporting[6]. Such pragmatic initiatives can inform future projects and regulatory frameworks to capture patient relevant outcomes within

[4] www.ctti-clinicaltrials.org, Database: http://feasibility-studies.ctti-clinicaltrials.org

proposed information and communication technologies for real-world evidence for clinical trials in dementia [80].

As the power of wearable data becomes evident, the accumulation of data by research groups should be made freely available and advertised to other researchers who may be able to offer new insights and analytical techniques. Barriers to data access should be minimised where possible as these valuable resources (often funded through public finances) present an immediate and pragmatic opportunity to move medicine in a new direction. Sole use of inertial wearables to remotely assess gait (and PC) are perhaps limited by contextual analysis, examining effect of environment of gait biomarker. Additional sensing technologies and modalities (including cameras [15] smart apparel [81] and implantables [82]) should be investigated for their ability to enhance clarity, data interpretation, ubiquity and to accelerate global uptake. Finally, wearables research to date has primarily focused on assessment. Future wearables research may increasingly focus on closing the loop by providing real time feedback and stimulation to improve gait and postural control [83, 84].

6.0 Conclusion

This review examines some of the recent develops with wearable technology to quantify PC and gait in those with dementia. To date there has been limited research conducted within this area but evidence suggests that pragmatic and patient centred assessments may be achieved beyond the clinic. Inertial wearables may offer new insights to dementia through their digital PC and gait digital biomarkers but further work is needed. The general deployment of wearables at scale remains technically (and financially) challenging but barriers may be reduced by learning from or taking guidance from organisations like CTTI and more improved mechanisms for data sharing amongst research groups. Digital PC and gait biomarkers from wearables potentially offer low-cost predictive sensing for those with dementia, prediction of cognitive decline years before clinical diagnosis.

Contributors

A Godfrey created the concept for the paper and contributed to the drafting of the paper.
M Brodie contributed to the concept of the paper and the drafting of the paper.
KS van Schooten contributed to the concept of the paper and the drafting of the paper.
M Nouredanesh provided guidance on the drafting of the paper and edited the draft version.
S Stuart provided guidance on the drafting of the paper and edited the draft version.
L Robinson provided guidance on the drafting of the paper and edited the draft version.
All authors reviewed the paper and provided input on each draft.

Conflict of interest

The authors declare that they have no conflict of interest.

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